Lecture #13
Spectral Editing

• Topics
  – Introduction
  – J-difference editing
  – Multiple quantum filtering

• Handouts and Reading assignments
  – de Graaf, Chapter 8.
  – van de Ven, 4.1, 4.2, 4.6, and 4.8
Introduction

• Even though, *in vivo* spectra are already simplified by concentration and relaxation time detection limits, there are nonetheless multiple overlapping peaks that can greatly complicate unambiguous peak assignments and quantification.

• In principle, spectral editing includes all techniques which can simplify a NMR spectrum, such as…
  – Water suppression
  – Spatial localization
  – TR/TE/TI variations

• We’ll define spectral editing in the more restrictive sense of only including those techniques which utilize J coupling between spins to discriminate among metabolites.
In Vivo $^1$H Spectrum

- We’ll focus on the $^1$H spectrum
  - High sensitivity
  - Small chemical shift range
  - Same hardware as MRI
  
  crowded $\Leftrightarrow$ rich

![In Vivo $^1$H Spectrum Diagram]
Solutions

• Fit everything
e.g. least squares fit using spectra of
in vitro metabolite solutions as basis
functions (see Provencher et al. MRM
30:672-9, 1993.)

• Increase $B_0$

• Collect full 2D NMR spectrum

• Edit/simplify 1D NMR spectrum
Refinements

• Strong versus weak coupling
  – In general, strong coupling requires considering the full density matrix
  – Weak coupling is appropriate to many in vivo applications (at least to a first approximation) and can be analyzed using the POF.

• Performance criteria
  – Sensitivity
  – Background discrimination \{ \text{CNR} \}
  – Robustness to motion-artifacts (single- vs multi-shot)
  – Relaxation time considerations

• Spatial encoding - to be added later (next couple of lectures)
J-Difference Editing

• Acquisition 1

\[ \hat{I}_z \rightarrow \hat{I}_y \rightarrow \hat{I}_y \cos \pi J(\frac{1}{2}) - 2 \hat{I}_x \hat{S}_z \sin \pi J(\frac{1}{2}) = -\hat{I}_y \]

• Acquisition 2

\[ \hat{I}_z \rightarrow \hat{I}_y \rightarrow \hat{I}_y \cos \pi J(\frac{1}{2} - \frac{1}{2}) - 2 \hat{I}_x \hat{S}_z \sin \pi J(\frac{1}{2} - \frac{1}{2}) = \hat{I}_y \]

• Algorithm: Edited signal = Acq2-Acq1
Example: Lactate-Lipid Discrimination

Spin echo:
Unedited spectrum

J=7 Hz

Acquisition 1:
Spin echo w/ nonselective 180

TE=144ms

Acquisition 2:
Spin echo w/ selective 180

Difference spectrum

Sum spectrum
MRSI with J-editing for Lactate

- MELAS patient (metabolic disorder with multiple strokes)

J-editing for GABA

GABA

$^{1}{H \text{ MRS}}$

J coupled

Phantom study

triplet

selective inversion

editing efficiency < 100%
J-editing for GABA

- 3 T In Vivo Brain Spectra
  Editing Off

Difference spectrum (w/ selective 180 centered at 1.9 ppm)
Parameters: TR/TE = 1500/68 ms, 18cc voxel, occipital lobe, 26 min acquisition, head coil

- Drug study
  anti-seizure drug

Note: quantitation complicated by some co-edited resonances
The Oversampled 2D-J Experiment

- J-difference editing is a special case of a full 2D-J acquisition

\[ \begin{align*}
\text{\(90^\circ \frac{t_1}{2}\)} & \quad \text{acquire} \\
\Omega_I, \Omega_I & \text{refocused} \\
\therefore \text{only } J \text{ evolution during } t_1 \\
\end{align*} \]

- Acquire data for multiple values of \( t_1 \). 2D-FFT yield 2D-J spectrum.

3 T “TE-averaged” Normal Gray Matter Spectrum

F1=0 spectra

In vivo

In vitro
The Oversampled 2D-J Experiment

Elevated choline

Breast cancer

Prostate
Summary: J-editing

• Positives
  – Simple, robust
  – High sensitivity
  – High specificity

• Negatives
  – Subtraction artifacts due to …
    … motion
    … hardware instabilities
    … minor differences in spin dynamics between pulse sequences (e.g. slice profiles)
Generic Multiple-Quantum Filter

- 180s used to refocus chemical shift
- Selection of coherences via phase cycling or use of gradients
DQ Filter - POF

- Consider a three spin system where $I$ and $S$ are J-coupled and $R$ is an uncoupled spin we wish to suppress (for now, assume $TM$ is very short).

\[ \hat{I}_z + \hat{S}_z + \hat{R}_z \]

\[ -(2\hat{I}_x \hat{S}_z + 2\hat{I}_z \hat{S}_x) + \hat{R}_y \]

antiphase

\[ -(2\hat{I}_x \hat{S}_y + 2\hat{I}_y \hat{S}_x) - \hat{R}_z \]

\[ (2\hat{I}_x \hat{S}_z + 2\hat{I}_z \hat{S}_x) - \hat{R}_y \]

antiphase

\[ \hat{I}_y + \hat{S}_y - \hat{R}_y \]

Only problem is that we haven’t really filtered out anything!
Phase Cycling

- One solution: cycle the phases of the first three RF pulses

Example of a 4-cycle experiment

<table>
<thead>
<tr>
<th>Experiment (1st three pulses)</th>
<th>$\hat{\sigma}$ after readout pulse</th>
<th>$\hat{\sigma}$ at data acquisition</th>
</tr>
</thead>
<tbody>
<tr>
<td>$90^\circ_x - \tau - 180^\circ_y - \tau - 90^\circ_x - \cdots$</td>
<td>$(2\hat{I}_x \hat{S}_z + 2\hat{I}_z \hat{S}_x) - \hat{R}_y$</td>
<td>$\hat{I}_y + \hat{S}_y - \hat{R}_y$</td>
</tr>
<tr>
<td>$90^\circ_y - \tau - 180^\circ_x - \tau - 90^\circ_y - \cdots$</td>
<td>$-(2\hat{I}_x \hat{S}_z + 2\hat{I}_z \hat{S}_x) - \hat{R}_y$</td>
<td>$-\hat{I}_y - \hat{S}_y - \hat{R}_y$</td>
</tr>
<tr>
<td>$90^\circ_{-x} - \tau - 180^\circ_y - \tau - 90^\circ_{-x} - \cdots$</td>
<td>$(2\hat{I}_x \hat{S}_z + 2\hat{I}_z \hat{S}_x) - \hat{R}_y$</td>
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</tr>
</tbody>
</table>

filter $= (1) - (2) + (3) - (4)$

- Problem: no longer single-shot editing
Gradients

• Consider the effect of the application of a gradient pulse on $\mathbf{\hat{\sigma}}$.

Assume the gradient is a $z$ gradient: $G_z$

The gradient adds to $B_0$ such that $\mathbf{\hat{H}}$ becomes a function of position.

$$\mathbf{\hat{H}}_G = -\gamma z \mathbf{\hat{I}}_z \int_0^T G_z(t) dt$$

• Example: $\mathbf{\hat{\sigma}}_1 = \mathbf{\hat{I}}_y$ and gradient area such that $\pi$ rads per unit $z$.

$$\mathbf{\hat{I}}_y \xrightarrow{\mathbf{\hat{I}}_z(\pi z)} \mathbf{\hat{I}}_y \cos \pi z + \mathbf{\hat{I}}_x \sin \pi z$$

...to get the total coherence, we would then need to integrate over $z$. 
DQ Filtering with Gradients

\[
\hat{\sigma} \text{ at various points in time (ignoring chemical shift terms) is …}
\]

1. \[-2 \hat{I}_x \hat{S}_y - 2 \hat{I}_y \hat{S}_x \xrightarrow{\hat{s}_z (\pi_2)} (2 \hat{I}_x \hat{S}_z + 2 \hat{I}_z \hat{S}_x) \cos 2\pi z + (-2 \hat{I}_x \hat{S}_z + 2 \hat{I}_z \hat{S}_x) \sin 2\pi z \]

2. \[
(-2 \hat{I}_x \hat{S}_y - 2 \hat{I}_y \hat{S}_x) \cos 2\pi z + (-2 \hat{I}_x \hat{S}_x + 2 \hat{I}_y \hat{S}_y) \sin 2\pi z
\]

3. This term involves unobservable MQ coherences and can be ignored (we are going to apply no more 90s so it will never evolve into transverse magnetization).

4. Integrating over z… \[
\frac{1}{2} (2 \hat{I}_x \hat{S}_z + 2 \hat{I}_z \hat{S}_x)
\]

5. \[
\frac{1}{2} (\hat{I}_y + \hat{S}_y) \quad \text{… a single-shot filter with 50\% yield.}
\]
DQ Filtering with Gradients

- Consider the following two DQ filters...

**DQ1:**

\[
(2\hat{I}_x\hat{S}_z + 2\hat{I}_z\hat{S}_x)\cos 2\pi \tau \rightarrow \frac{1}{2}(2\hat{I}_x\hat{S}_z + 2\hat{I}_z\hat{S}_x) \cos^2 2\pi \tau + (\hat{I}_y + \hat{S}_y)\sin 2\pi \tau \cos 2\pi \tau
\]

Integrating over \(z\)...

**DQ2:**

\[
(2\hat{I}_x\hat{S}_z + 2\hat{I}_z\hat{S}_x)\cos 2\pi \tau \rightarrow (2\hat{I}_x\hat{S}_z + 2\hat{I}_z\hat{S}_x)\cos^2 2\pi \tau - (\hat{I}_y + \hat{S}_y)\sin 2\pi \tau \cos 2\pi \tau
\]

Integrating over \(z\)...

**Acquire**
Example: Glutamate DQF

- **E**: NAA Simulation
  - X of ABX

- **D**: Gln Simulation
  - A of AMNPQ
  - MNPQ of AMNPQ

- **C**: Glu Simulation
  - A of AMNPQ
  - MNPQ of AMNPQ

- **B**: Combined Simulations

- **A**: Human Brain Experiment

4.5 4 3.5 3 2.5 2
Lactate Imaging using a DQF

inject tumor cells
wait 1-2 weeks
scan using DQF-MRI

N
RF coil
S

Live mouse

Mouse died during study

Aren’t lipids also J-coupled? Shouldn’t subcutaneous lipid signals be much larger than that due to lactate?

Heterogeneous lactate distribution within tumor

water

lactate

water

lactate

lipid
Summary

- Wide variety of spectral editing techniques available
- Optimum choice depends on application
- Some factors to consider:
  - Required quantitative accuracy
    - Absolute versus relative quantitation
    - Sensitivity
  - Robustness
    - $B_0$ inhomogeneity
    - $B_1$ inhomogeneity
    - Patient motion
Next Lecture: In vivo MRS-detectable metabolites